

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1.-55. (Cancelled)

56. (Currently amended) A substrate for analyzing a nucleic acid, the substrate comprising:

a cavitated fiber optic wafer formed from a fused bundle of a plurality of individual optical fibers, each individual optical fiber having a diameter between 3 and 100  $\mu\text{m}$ , the wafer comprising a top surface and a bottom surface, the top surface comprising at least 10,000 wells, wherein said wells are etched into the top surface of the cavitated fiber optic wafer and wherein the thickness of the wafer between the top surface and the bottom surface is between 0.5 mm and 5.0 mm in thickness; wherein the depth of each well ranges from between one half the diameter of an individual optical fiber and three times the diameter of an individual optical fiber; and wherein a plurality of wells on the top surface of the cavitated wafer have a nucleic acid ~~disposed~~ therein; and

a plurality of beads ~~disposed~~ within wells on the top surface of the cavitated wafer, said beads having a pyrophosphate sequencing reagent attached thereto.

57. (Previously amended) The substrate of claim 56, wherein the nucleic acid is immobilized on the wells or on said beads.

58. (Previously amended) The substrate of claim 56, wherein the diameter of each individual optical fiber in the cavitated wafer is between 6-50  $\mu\text{m}$ .

59. (Previously amended) The substrate of claim 58, wherein the fiber optic surface includes two or more nucleic acids separated by approximately 10  $\mu\text{m}$  to approximately 200  $\mu\text{m}$ .

60. (Previously amended) The substrate of claim 58, wherein the fiber optic surface includes two or more nucleic acids separated by approximately 10  $\mu\text{m}$  to approximately 150  $\mu\text{m}$ .

61. (Previously amended) The substrate of claim 58, wherein the fiber optic surface includes two or more nucleic acids separated by approximately 150  $\mu\text{m}$ .

62.-63. (Cancelled)

64. (Previously amended) The substrate of claim 56 wherein the wafer further comprises  $10^3$  or more groups of nucleic acid sequences in said wells.

65. (Previously amended) The substrate of claim 64, wherein said substrate comprises  $10^4$  or more different groups of nucleic acid sequences in discrete known regions.

66. (Previously amended) The substrate of claim 64, wherein said substrate comprises  $10^5$  or more different groups of nucleic acid sequences in discrete known regions.

67. (Previously amended) The substrate of claim 64, wherein the nucleic acid sequences are attached to the wells or beads by a linker.

68. (Previously amended) The substrate of claim 64, wherein the nucleic acid sequences are covalently attached to the wells or beads.

69.- 83. (Cancelled)

84. (Currently amended) An apparatus for processing a plurality of nucleic acids, the apparatus comprising:

a flow chamber having disposed therein a cavitated fiber optic wafer;

a cavitated fiber optic wafer formed from a fused bundle of a plurality of individual optical fibers, each individual optical fiber having a diameter between 3 and 100  $\mu\text{m}$ , the wafer comprising a top surface and a bottom surface, the top surface comprising at least 10,000 wells, wherein said wells are etched into the top surface of the cavitated fiber optic wafer and wherein the thickness of the wafer between the top surface and the bottom surface is between 0.5 mm and

5.0 mm in thickness; wherein the depth of each well ranges from between one half the diameter of an individual optical fiber and three times the diameter of an individual optical fiber; and wherein a plurality of wells on the on the top surface of the cavitated wafer have a nucleic acid ~~disposed~~ therein;

a plurality of beads ~~disposed~~ within wells on the top surface of the cavitated wafer, said beads having a pyrophosphate sequencing reagent attached thereto;

fluid means for delivering additional pyrophosphate sequencing reagents, including sequential delivery of nucleotide triphosphates, from one or more reservoirs to the flow chamber so ~~the~~ nucleic acids ~~disposed on beads~~ in the wells on the top surface of the fiber optic wafer are exposed to the reagents; and

detection means for detecting optical signals from each well, wherein said detection means is in communication with the wells, each optical signal being indicative of reaction of the pyrophosphate sequencing reagents with the nucleic acid in a well.

85. (Previously amended) The apparatus of claim 84, wherein the diameter of each individual optical fiber in the cavitated wafer is between 6-50  $\mu\text{m}$ .

86. (Previously amended) The apparatus of claim 85, wherein said detection means is a CCD camera.

87. (Previously amended) The apparatus of claim 84, wherein the nucleic acid is DNA.

88. (Previously amended) The substrate of claim 56 wherein the substrate has a polished fiber optic surface opposite to the cavitated fiber optic surface.

89. (Previously added) The substrate of claim 88 wherein the polished surface allows for optical coupling to a second optical fiber.

90. (Previously amended) The substrate of claim 56 wherein the cavitated fiber optic wafer is coated.

Applicants: Rothberg, et al.  
U.S.S.N. 09/814,338

91. (Previously added) The substrate of claim 90 wherein the coating is selected from the group consisting of plastic, gold layers, organosilane reagents, photoreactive linkers, hydrophilic polymer gels and pluronic polymers.

92. (Currently amended) The substrate of claim 56 wherein said pyrophosphate sequencing reagent is luciferase.

93. (Currently amended) The substrate of claim 56 wherein said pyrophosphate sequencing reagent is sulfurylase.

94.-95. (Cancelled)

96. (Previously amended) The apparatus of claim 84 wherein the cavitated fiber optic wafer is coated.

97. (Previously amended) The apparatus of claim 96 wherein the coating is selected from the group consisting of plastic, gold layers, organosilane reagents, photoreactive linkers, hydrophilic polymer gels and pluronic polymers.

98. (Previously amended) The apparatus of claim 84 wherein said pyrophosphate sequencing reagent is luciferase.

99. (Previously amended) The apparatus of claim 84 wherein said pyrophosphate sequencing reagent is sulfurylase.

100. (New) The apparatus of claim 84, wherein the nucleic acid is immobilized on the wells or on said beads.